

Early Detection And Prevention Of Oral Cancer

Ameer Alturfi¹, Zahraa Amer Tawfeeq², Husam Abdulabbas Mutasher³, Abeer Ahmed Akhmais⁴, Mohammed Dhyeaa⁵

¹College of Dentistry University of Mashraqameer.a.abdulhassan@uom.edu.iq

²College of Dentistry University of Mashreq Ion.za.pre92@gmail.com

³B.D.S, M.Sc., Oral and Maxillofacial Surgery Lecturer Department of Oral & Maxillofacial Surgery, College of Dentistry, Al Kut university, Wasit, 52001, Iraqhusam.mohammed@uokut.edu.iq

⁴Pharmacist at the Iraqi Ministry of Health abeerahmed00010@gmail.com

⁵Pharmacist mohammeddiaa85@yahoo.com

Abstract

Oral cancer remains a critical global health concern characterized by high morbidity and mortality rates, primarily due to delayed clinical presentation. This theoretical research examines the conceptual foundations of early detection and the strategic implementation of preventive measures. By analyzing existing literature, the study explores the progression of oral potentially malignant disorders (OPMDs) and evaluates the systemic barriers to early diagnosis. The research highlights the significance of clinician-patient education and the integration of diagnostic protocols in reducing the disease burden. Ultimately, this study argues that a paradigm shift from reactive treatment to proactive prevention—centered on risk factor modification and rigorous screening frameworks—is essential for improving long-term survival outcomes and public health efficacy.

Keywords: Oral Cancer, Early Detection, Prevention Strategies, Oral Potentially Malignant Disorders (OPMDs), Risk Factors,

1.INTRODUCTION

Oral cancer is a global public health issue and remains one of the leading causes of death due to oral diseases. It includes cancers of the lips, various parts of the mouth, and the oropharynx (WHO, 2023). According to the International Classification of Diseases for Oncology (ICD-O), oral cancer is classified into two distinct types: oral cavity cancer (OCC), also known as "mouth cancer," and oropharyngeal cancer (OPC), or "throat cancer". The United States National Institute of Health (2023) defines oral cancer as cancers affecting both the mouth and the back of the throat. Specifically, it refers to cancers that develop on the tongue, the tissue lining the mouth and gums, under the tongue, at the base of the tongue, and in the area of the throat at the back of the mouth[1].

However, recent research suggests that carcinoma of the mouth (oral cancer) should be considered a separate disease from carcinoma originating in the oropharynx. This distinction is made because oropharyngeal cancer is primarily linked to human papillomavirus (HPV) infection, whereas oral cancer is more commonly associated with traditional risk factors such as tobacco and alcohol use [2]. Additionally, the FDI World Dental Federation defines oral cancer as malignancies, predominantly squamous cell carcinomas, that are highly lethal, disfiguring, and incapacitating. This includes malignancies of the vermilion borders of the lips and all surfaces of the oral cavity, including the anterior two thirds of the tongue[3].

Any oral lesion that does not resolve within two to three weeks should raise suspicion for the treating clinician. Lesions that are exophytic, proliferative, or papillomatous can also be indicative of oral cancer. Furthermore, a non-healing extraction socket (lasting more than 6 weeks) should be

considered suspicious for a potential alveolar carcinoma. Oral cancers, aside from squamous cell carcinoma (SCC), may manifest as pigmented lesions.

1.2. Epidemiology

According to data from the Global Cancer Observatory (GLOBOCAN), in 2020, there were 377,713 new cases of oral cancer diagnosed worldwide, along with 177,757 deaths from the disease. The incidence rate was higher in men (6.0 per 100,000) compared to women (2.3 per 100,000) [4]. Regionally, oral cancer ranks as the 11th most common malignancy in Asia and the 4th in Southeast Asia, with 166,900 new cases reported in 2020 [5, 6]. In Southeast Asia, oral cancer is the 5th most common cause of cancer-related death, following lung, breast, cervix, and liver cancers, with 92,418 deaths reported in 2020 [6]. In Malaysia, there were 742 new cases and 403 deaths in 2020, and the number of prevalent cases over a five-year period was 2,199 [4]. Oral cancer is particularly common among the Indian ethnic group, ranking 6th in Indian females and 12th in Indian males. The prevalence of oral cancer detected at Stage I ranges from 10% to 30% across various sites, including the lips, tongue, and mouth [7].

1.3. Clinical Management

Oral cancer typically presents as abnormalities in the oral cavity, including the soft palate, alveolar ridge, retromolar trigone, buccal mucosa, lips, tongue, floor of the mouth, and rigid palate. Patients may also experience loose teeth, bleeding, discomfort or numbness in the mouth or face, difficulty with dental prostheses, and a sudden unexplained weight loss. The most common presentation is an ulcerated lesion in the oral cavity. Other signs that may suggest oral cancer include white lesions, erythematous lesions, exophytic growths, proliferative lesions, or papillomatous formations [8]. A tissue biopsy from the suspicious area is essential for confirming the diagnosis. Diagnosing oral cancer requires a comprehensive head and neck examination, including precise measurement, palpation to assess lesion thickness, clinical evaluation of cervical lymph nodes, and radiological imaging [8]. Surgery remains the primary treatment for most oral cancers, with the goal of removing the cancer, preserving or restoring the affected area's shape and function, minimising treatment side effects, and preventing the development of new malignancies [9]. Since the 1970s, the prognosis for oral cancer has improved significantly, largely due to the increased use of adjuvant therapies and chemoradiotherapy [10]. Over the past three decades, the age-standardised incidence of oral cancer has steadily risen worldwide, while age-standardised mortality has declined [11]. This suggests that advancements in treatment and technology have contributed to longer survival rates, leading to an increase in the number of survivors. However, patients may still be affected by the clinical symptoms of oral cancer and the side effects of treatment, which can significantly impact their quality of life [12].

1.4. Risk Factors

Oral cancer is a multifactorial condition influenced by various risk factors, including harmful lifestyle behaviours such as tobacco smoking, betel quid chewing, and alcohol consumption [13, 14, 15]. Betel quid chewing, especially when combined with tobacco use, significantly increases the risk of oral cancer, with studies showing a threefold increase in certain populations and a five- to eightfold increase in others [16]. Consuming more than 50 grams of alcohol daily has been linked to a sevenfold rise in oral cancer risk in specific demographic groups [17]. Additionally, the combined effects of tobacco smoking, alcohol consumption, and betel quid chewing further amplify the risk of oral cancer [18]. Emerging evidence strongly suggests a causal link between HPV and certain types of oral cancer, particularly those affecting the tongue and tonsils, which are more common in young individuals with no history of tobacco or alcohol use. In addition to behavioural risk factors, other factors such as socioeconomic status, occupational exposures, and genetic predisposition have also been found to increase the likelihood of developing oral cancer [19, 20, 21, 22, 23, 24, 25].

1.5. Genetic and oral cancer

Carcinogenesis is a complex, multi-process in which genetic events within signal transduction pathways governing normal cellular physiology are quantitatively altered [26]. The genetic basis of

cancer is now well-established. Under normal conditions, these tightly controlled excitatory and inhibitory pathways regulate oral keratinocyte biology. Basic cellular functions under these controls include cell division, differentiation, senescence and adhesion. These regulatory pathways are composed of extra cellular ligands which bind to cell-surface receptors to generate intracellular signals sent through secondary messengers.

These signals either directly alter cell function or stimulate the transcription of genes whose proteins effect changes[27]. Cancer is the result of an accumulation of changes in the excitatory and inhibitory cellular pathways, which may occur at any level of a given pathway. It has been estimated that from three to six somatic mutations are needed transform a normal cell into its malignant counterpart[26].

As the cell accumulates these alterations or mutations, it becomes functionally independent from the surrounding oral epithelium made up of normal cellular functions tightly controlled by these regulatory pathways are subverted in tumor cells, thus enhancing the ability to proliferate, stimulate neo-vascularization and grow by invading locally or metastasizing to distant sites[34]. The histologic progression of oral carcinogenesis is believed to reflect the accumulation of these changes[28]. Genetic damage in oral cancer cells can be divided into 2 categories. Dominant changes most frequently occurring in proto-oncogenes but also in certain tumor suppressor genes (TSGs) result in gain of function. Recessive changes, mutations most frequently noted in the growth-inhibitory pathway genes or commonly in TSGs, cause loss of function[27].

1.6. Diagnosis of oral cancer

Early Diagnosis Is the Key to Enhancing Patient Survival.

Signs & Symptoms of Oral Cancer is important in diagnosis , The most common signs & symptoms of oral cancer include : [29]

Red or red and white, patches on the lining of mouth or tongue.-

Leukoplakia > 2cm in size.-

One or more mouth ulcers that do not heal after three weeks-

Swelling in mouth that lasts for more than three weeks-

Pain when swallowing (dysphagia)-

-Difficulty chewing, swallowing, speaking or moving tongue.

Difficulty in opening mouth, moving jaw, or swelling or pain in jaw.-

A persistent pain in the neck-

A hoarse voice-

Unexplained weight loss-

Unusual changes in sense of taste-

Difficulty in tolerating spicy foods-

Excessive salivation-

Pain in ear-

The lymph nodes (glands) in neck become swollen-

Oral cancer is diagnosed on the basis of routine visual physical examination ,medical history and risk factors probing. Early-stage diagnosis and prompt referral to specialist hospitals is a crucial factor in increasing the patients' survival rate of up to 90%. Unfortunately, about 60% of oral cancers are diagnosed at advanced stages III or IV with metastasis leading to a higher mortality rate [30].

Diagnostic delays may be attributed to both patients' ignorance as well as the ignorance of heOral cancer is diagnosed on the basis of routine visual physical examination medical history and risk factors probing. Early-stage diagnosis and prompt, referral to specialist hospitals is a crucial factor in increasing the patients' survival rate of up to 90%. Unfortunately, about 60% of oral cancers are diagnosed at advanced stages III or IV with metastasis leading to a higher mortality rate [30].Diagnostic delays may be attributed to both patients' ignorance as well as the ignorance of health care professionals[31].

The delaying factors on the patients' behalf include late perception of the lesion or symptoms as oral cancers are mostly asymptomatic, ignoring the lesions, self- medications, fear of surgery, poor socio-economic conditions and little or no access to specialized healthcare[32]. On the professional side, the factors include improper intra-oral and extra-oral examination, delay in biopsy taking, or wrongful biopsy site selection for histopathological examination. The average delay for the initial to definite diagnosis is reported to be about 6 months [33]. Population targeted educational intervention should mainly focus on the high-risk groups. The professional educational interventions, on the other hand, should include a sound knowledge of the disease presentation, specifically on sites like gingivae, floor of the mouth, and retromolar trigone. Screening programs should also be implemented in every country at primary or the secondary care level.

The use of social media and mobile apps can be beneficial for population targeted oral cancer symptoms awareness programs [29]. A dentist or medical doctor may check the oral cavity during a routine check- up. The exam will include looking for lesions, including areas of Leukoplakia (an abnormal white patch of cells) and erythroplakia (an abnormal red patch of cells). Leukoplakia and erythroplakia lesions on the mucous membranes may become cancerous. More than half of oral cancers have already spread to lymph nodes or other areas by the time they are found.

1.7 Prevention Strategies

Oral cancer has one of the lowest survival rates when detected at advanced stages. Delayed diagnosis and ineffective treatment at later stages of the disease have been linked to poor survival outcomes in oral cancer cases [35, 36,37]. The primary factors contributing to delayed diagnosis include a lack of awareness among patients about the risk factors and symptoms of oral cancer, inaccurate clinical judgement by attending physicians or dentists, and long waiting times to access healthcare services [38,39]. The longer the delay in diagnosis, the more likely the cancer will progress to an advanced stage, requiring more extensive treatment, leading to a poorer prognosis and increased psychological distress[40,41,42]. Previous studies have shown that early detection and prevention of OPMD can lead to a better prognosis and improve the survival rates of those who develop oral cancer [43, 44]. Since the oral cavity is an accessible anatomical region for examination by dentists, physicians, and even individuals themselves, regular dental check- ups and awareness of the signs and symptoms of oral cancer are critical for early detection[45,46]. Mouth Self-Examination (MSE) is a valuable tool for early detection, reducing the time between detecting oral lesions and initiating treatment, thus allowing for preventive measures and raising awareness about the disease. It empowers individuals to recognise symptoms and seek help sooner [47, 48].

Both prevention and screening of oral cancer are widely recognised as essential, and early diagnosis can lead to less aggressive treatment, improving not only the quality of life but also the overall 5-year survival rate[44]. Opportunistic mass screening is an effective strategy to detect oral cancer in its precancerous or early stages, where survival rates are higher, and it has proven to be cost-effective [49].

However, when screening is limited to high-risk individuals, those who are not classified as high risk may be missed and not screened [50]. In 2022, the OHP MOH strengthened its Primary Prevention and Early Detection of OPMD

and Oral Cancer Programme through collaboration with relevant agencies. To increase the number of people screened for oral cancer, all new patients aged 18 and above who attend dental check-ups will be screened for oral lesions (opportunistic screening). If an oral lesion is suspected to be an OPMD or oral cancer, the patient will be referred to a dental specialist for further assessment or investigation. The attendance of referred patients to specialist clinics and their diagnoses will be tracked. High-risk communities, based on widespread prevalence of high-risk habits or identified cancer cases, will be visited once every five years (OHP, 2018). However, identifying high-risk communities is challenging, as oral cancer cases are no longer confined to known groups, such as estate workers. Therefore, efforts are being made to emphasise mouth self-examination to help individuals identify any abnormalities in their mouths. Although early detection of oral cancer

significantly improves survival, over 60% of oral cancer cases in Malaysia are detected at later stages, meaning more than 50% of oral cancer patients do not survive beyond five years (Ministry of Health, 2019). While oral cancer is one of the few cancers that are visibly detectable, missed opportunities stem for early detection from low awareness of the disease and limited access to specialised healthcare for early

1.8.diagnosis and treatment

Advancements in technology, such as mobile applications, offer a promising solution for enhancing early detection and management of oral cancer. However, issues related to data privacy, accuracy, and equitable access must be addressed to maximise their impact [51].

Conclusion:

The revised guidelines for the oral cancer programme aim to strengthen the of implementation the Primary Prevention and Early Detection of Oral Potentially Malignant Disorders and Oral Cancer Programme by addressing previous shortcomings. These improvements focus on enhancing early detection, improving data management, strengthening referral pathways increasing collaboration, and promoting education and awareness.

REFERENCES:

- 1.National Cancer Institute. National Institute of Health. U.S. Department of Health and Human Services. Oral Cancer retrieved online on 1 Nov 2024).
- 2.Speight, P. M., & Farthing, P. M. (2018). The pathology of oral cancer. *British dental journal*, 225(9), 841-847).
- 3.FDI World Dental Federation. Policy Statement on Oral Cancer. September 2015
- 4.International Agency for Research on Cancer. (2022a). The Global Cancer Observatory Asia2020. Retrieved from <https://gco.iarc.fr/today/data/factsheets/populations/935-asia-fact-sheets.pdf>
- 5.International Agency for Research on Cancer. (2022b). The Global Cancer Observatory 2020: Lip, oral cavity. Retrieved from <https://gco.iarc.fr/today/data/factsheets/cancers/1-Lip-oral-cavity-fact-sheet.pdf>
- 6.International Agency for Research on Cancer. (2022c). The Global Cancer Observatory 2020: Malaysia. Retrieved from <https://gco.iarc.fr/today/data/factsheets/populations/458-malaysia-fact-sheets.pdf>
7. Malaysia National Cancer Registry Report 2012-2016 (check citation
- 8.Wong, T. S. C., & Wiesenfeld, D. (2018). Oral cancer. *Australian Dental Journal*, 63, S91-S99
- 9.Shah, J. P., & Gil, Z. (2009). Current concepts in management of oral cancer–surgery.*Oral Oncology*, 45(4), 394-401
- 10.Cheraghlou, S., Schettino, A., Zogg, C. K., & Judson, B. L. (2018). Changing prognosis of oral cancer: An analysis of survival and treatment between 1973 and 2014. *The Laryngoscope*, 128(12), 2762-2769.
- 11.Stewart, B. W., & Wild, C. P. (2014). *World cancer report 2014*. World Health Organization
- 12.Valdez, J. A., & Brennan, M. T. (2018). Impact of oral cancer on quality of life. *Dental Clinics of North America*
13. Choi SY, Kahyo H. Effect of cigarette smoking and alcohol consumption in the aetiology of cancer of the oral cavity, pharynx and larynx. *Int J Epidemiol*. 1991;20 (4): 878 -885.
- 14.(4).. Balaram, P., Sridhar, H., Rajkumar, T., Vaccarella, S., Herrero, R., Nandakumar, Franceschi, S. (2002). Oral cancer in southern India: the influence of smoking, drinking, paan-chewing, and oral hygiene. *Int J Cancer* 98(3), 440-445.

15. Radoi, L., Paget-Bailly, S., Cyr, D., Papadopoulos, A., Guida, F., Schmaus, Luce, D. (2013). Tobacco smoking, alcohol drinking and risk of oral cavity cancer by subsite: results of a French population-based case-control study, the ICARE study. *Eur J Cancer Prev*, 22(3), 268-276.
16. Subapriya, R., Thangavelu, A., Mathavan, B., Ramachandran, C. R., & Nagini, S. (2007). Assessment of risk factors for oral squamous cell carcinoma in Chidambaram, Southern India: a case-control study. *Eur J Cancer Prev*, 16(3), 251-256.
17. Moreno-Lopez, L. A., Esparza-Gomez, G. C., Gonzalez-Navarro, A., Cerero-Lapiedra, R., Gonzalez-Hernandez, M. J., & Dominguez-Rojas, V. (2000). Risk of oral cancer associated with tobacco smoking, alcohol consumption and oral hygiene: a case-control study in Madrid, Spain. *Oral Oncol*, 36(2), 170-17
18. Petti, Masood, & Scully, 2013, The Magnitude of Tobacco Smoking-Betel Quid Chewing- Alcohol Drinking Interaction Effect on Oral Cancer in South-East Asia. A Meta-Analysis of Observational Studies, *PLoS One*. 2013; 8(11): e7899
19. Conway, D. I., Petticrew, M., Marlborough, H., Berthiller, J., Hashibe, M. and Macpherson, L. M.D. (2008), Socioeconomic inequalities and oral cancer risk: A systematic review and meta-analysis of case-control studies. *Int. J. Cancer*, 122: 2811–2819. doi:10.1002/ijc.2343
20. Rajkumar, T., Sridhar, H., Balaram, P., Vaccarella, S., Gajalakshmi, V., Nandakumar, A., Weiderpass, E. (2003). Oral cancer in Southern India: the influence of body size, diet, infections and sexual practices. *Eur J Cancer Prev*, 12(2), 135- 14
21. Chi, A. C., Day, T. A., & Neville, B. W. (2015). Oral cavity and oropharyngeal squamous cell carcinoma—an update. *CA Cancer J Clin*, 65(5), 401-421. doi:10.3322/caac.2129
22. Irani S. Distant metastasis from oral cancer: A review and molecular biologic aspects. *J Int Soc Prev Community Dent*. 2016;6:265–71
23. Agrawal et al. (2013); UV Radiation Increases Carcinogenic Risks for Oral Tissues Compared; <https://doi.org/10.1111/php.1214>
24. Llewellyn CD, Johnson NW, Warnakulasuriya KA. Risk factors for squamous cell carcinoma of the oral cavity in young people—a comprehensive literature review. *Oral Oncol*. Jul 2001;37(5): 401-41
25. Zain RB, Ikeda N, Razak I, et al. A national epidemiological survey of oral mucosal lesions in Malaysia. *Community Dent Oral Epidemiol*. 1997; 25: 377-83. 3012.0 APPENDICES1) 2) 3) 4) 5) Flo
26. Vogelstein B, Kinzler KW. The multistep nature of cancer. *Trends Genet*. 2019;9:138–41. [PubMed] [Google Scholar]
27. Bishop JM. Molecular themes in oncogenesis. • *Cell*. 2019;64:235–48. [PubMed] [Google Scholar]
28. Vokes EE, Weichselbaum RR, Lippman SM, Hong WK. Head and neck cancer. *N Engl J Med*. 2018;328:184–94. [PubMed] [Google Scholar]
29. Gomes MS, Bonan PR, Ferreira VY, de Lucena Pereira L, Correia RJ, da Silva Teixeira HB, et al. Development of a mobile application for oral cancer screening. *Technol Health Care*. (2017) 25:187–95. doi: 10.3233/THC-161259
30. Seoane-Romero J-M, Vázquez-Mahía I, Seoane J, Varela-Centelles P, Tomás I, López- Cedrún J-L. Factors related to late stage diagnosis of oral squamous cell carcinoma. *Med Oral Patol Oral Cirugia Bucal*. (2019) 17:e35–40. doi: 10.4317/medoral.17399
31. Sujir N, Ahmed J, Pai K, Denny C, Shenoy N. Challenges in early diagnosis of oral cancer cases series. *Acta Stomatol Croatica*. (2019) 53:174–80. doi: 10.15644/asc53/2/10
32. Jafari A, Najafi S, Moradi F, Kharazifard M, Khami M. Delay in the diagnosis and treatment of oral cancer. *J Dentist*. (2018) 14:146–50.
33. Epstein JB, Gorsky M, Cabay RJ, Day T, Gonsalves W. Screening for and diagnosis of oral premalignant lesions and oropharyngeal squamous cell carcinoma: role of primary care physicians. *Can Fam Phys Med Fam Can*. (2018) 54:870–5.
34. Weiner T, Cance WG. Molecular mechanisms involved in tumorigenesis and their surgical implications. *Am J Surg*. 2017;167:428–34. [PubMed] [Google Scholar]
35. Brocklehurst, P., Kujan, O., O'Malley, L. A., Ogden, G., Shepherd, S., & Glenny, A. M. (2013).

Screening programmes for the early detection and prevention of oral cancer. Cochrane Database Syst Rev, 11

- 36.. Grønhøj C, Jensen D, Dehlendorff C, et al. Impact of time to treatment initiation in patients with human papillomavirus-positive and -negative oropharyngeal squamous cell carcinoma. ClinOncol (R Coll Radiol). 2018;30(6):375–381.
37. Schutte HW, Heutink F, Wellenstein DJ, et al. Impact of time to diagnosis and treatment in head and neck cancer: a systematic review. Otolaryngol Head Neck Surg. 2020;162(40):446–457.
38. Basharat S, Shaikh BT, Rashid HU, Rashid M. Health seeking behaviour, delayed presentation and its impact among oral cancer patients in Pakistan: a retrospective qualitative study. BMC health services research. 2019; 19:1-9.
39. Badri P, Baracos V, Ganatra S, Lai H, Samim F, Amin M. Retrospective study of factors associated with late detection of oral cancer in Alberta: A qualitative study. Plos one. 2022;17(4).
40. Scully C, Kirby J. Statement on mouth cancer diagnosis and prevention. BrDent J. 2014;216(1):37.
41. Stefanuto, P., Doucet, J. C., & Robertson, C. (2014). Delays in treatment of oral cancer: a review of the current literature. Oral surgery, oral medicine, oral pathology and oral radiology, 117(4), 424-429.
42. Rakhmania, H., & Sufiawati, I. (2017). Impact of delay on diagnosis and treatment of oral squamous cell carcinoma: Three cases report. Journal of International Dental and Medical Research, 10(3), 1017-1020
43. Speight, P. M., & Farthing, P. M. (2018). The pathology of oral cancer. British dental journal, 225(9), 841-847
44. Awan Kh. Oral Cancer: Early Detection is Crucial. J Int Oral Health. 2014 Sep;6(5). > 45. Semple CJ, McCaughan E. Family life when a parent is diagnosed with cancer: impact of a psychosocial intervention for young children. Eur J Cancer Care (Engl). 2013;22(2):219-231.
46. Gómez I, Warnakulasuriya S, Varela-Centelles PI, et al. Is early diagnosis of oral cancer a feasible objective? Who is to blame for diagnostic delay?. Oral Dis. 2010;16(4):333-342.
47. Elango, K. J., Anandkrishnan, N., Suresh, A., Iyer, S. K., Ramaiyer, S. K., & Kuriakose, M. A. (2011). Mouth self-examination to improve oral cancer awareness and early detection in a high-risk population. Oral Oncology, 47(7), 620–624.
48. Sankaranarayanan R, Ramadas K, Thomas G, et al. Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomised controlled trial. Lancet. 2005; 365(9475): 1927-1933.
49. Warnakulasuriya S, Kerr AR. Oral Cancer Screening: Past, Present, and Future. J Dent Res. 2021 Nov;100(12):1313-1320. doi: 10.1177/00220345211014795. Epub 2021 May
50. Subramanian S, Sankaranarayanan R, Bapat B, Somanathan T, Thomas G, Mathew B, Vinoda J & Ramadas K. Cost-effectiveness of oral cancer screening: results from a cluster randomized controlled trial in India. Bulletin of the World Health Organization. 2009; 87: 200-206.
51. Topol, E. J. (2019). High-performance medicine: the convergence of human and artificial intelligence. Nature Medicine, 25(1), 44–56